Annotation

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Aerosol Therapy in Cystic Fibrosis

An aerosol is defined as a suspension of liquid or solid particles in air or oxygen, and the process of forming an aerosol is called nebulization. Therapeutically an aerosol may be inhaled and may, but does not necessarily, contain mucolytic, therapeutic, or antibiotic agents. Common usage of aerosol in medicine usually means intermittent inhalation by face mask or oral tube. Mist tents are aerosols given for prolonged periods in an enclosed space.

Particles are deposited in the airways by sedimentation, impaction, or diffusion, depending on the size and density of the particles. Large particles have a high rate of sedimentation or impaction, while small particles diffuse rapidly. Deposition of particles in the lung depends also on the dimension of the airways and the nature of airflow in them. Particles have to be less than 10μ to be deposited in the bronchioles and bronchi. Large inhaled particles are trapped in the upper airways, but it does not follow that therapy can be directed to a particular site in the lung by choosing particle size. Using technesium-labelled water aerosol produced by jet and ultrasonic nebulizers it has been shown, in adults with normal nasal breathing, that as much as 90% was deposited in the upper respiratory tract, but when breathing by a mouth tube only 50% was deposited in the upper respiratory tract. The volume of water that could be deposited in 24 hours in the lower respiratory tract of an adult with normal nasal or mouth breathing was about 6 ml. with the jet, and about 50 ml. using ultrasonic nebulizers (Wolfsdorf, Swift, and Avery, 1969).

The basic genetic defect in cystic fibrosis (CF) has not yet been clarified, but the majority of patients with this disorder eventually show progressive pulmonary disease. Various assumptions have been made based on pathological and physiological findings, and upon these regimens of treatment have been suggested. These patients have abnormal secretion from mucous glands in the tracheo-bronchial tree; the secretions accumulate; obstruction and infection follow leading to lung damage. Nevertheless, mucous gland hypertrophy in the absence of infection is not apparent in the lungs of infants dying from complications of meconium ileus (Reid and De Haller, 1964; Claireaux, 1956), nor has physicochemical analysis of tracheo-bronchial secretions shown any abnormality of the glycoproteins. Recent studies (Sturgess and Reid, 1969) have compared the viscosity of sputum from patients with chronic bronchitis with that from patients with CF: the viscosity of specimens from the two groups both for mucoid and purulent sputa was similar, but the purulent specimens were more viscid than the mucoid in both groups. By definition, 'normals' do not produce sputa, so comparison with normal tracheobronchial secretions has not been made.

The mechanism which may trigger the production of mucus in CF patients is not yet known. A high proportion (about 70%—personal observation) of CF infants presenting with respiratory symptoms carry *Staphylococcus pyogenes* on pharyngeal culture, but other bacterial or viral infection may play a major part in the triggering mechanism in the tracheo-bronchial tree. This has led to the use of antibiotics therapeutically and prophylactically, and over the years these have seemingly led to progressive improvement in prognosis.

The idea of mist therapy has received much support over the past 10 years from CF organizations in the USA and it features quite prominently in the regimen of treatment at present recommended by the National Cystic Fibrosis Research Foundation. Particular emphasis has been put on the use of mist tents at night. It was argued that this would help to thin mucous secretions, and so aid clearing of the lungs. In 1965 Doershuk *et al.* using such a regimen reported a 4½-year follow-up of patients in Cleveland, showing not only that patients who had no significant pulmonary involvement had been maintained in this state, but also that the progression of the disease in others had been slowed down. In 1967, a further study (Matthews, Doershuk, and Spector, 1967) before

and after mist tent therapy (using the jet type nebulizer) showed that abnormalities in vital capacity, functional residual capacity, residual volume, and residual volume/total lung capacity ratio improved towards normal while in the mist tent, but regressed again when the tent was removed.

Assuming that small particles get to smaller airways, and that if an aerosol contains a high proportion of smaller particles the results of treatment might be further improved, the ultrasonic nebulizer was introduced. This produced particles of the same size as the jet type, but in a denser cloud. A further study of patients (Doershuk *et al.*, 1968) with irreversible pulmonary damage, substituting an ultrasonic for the jet type nebulizer and comparing pulmonary function tests before and after the change, showed even further improvement. Consequently, they considered that, for short-term treatment of those CF patients with advanced disease, aerosol from an ultrasonic nebulizer was superior. However, in a further follow-up Matthews *et al.* (1968) reported that while at 12 months VC, FRC, RV, and MBC had all improved, this improvement was lost at 18 months, and by 24 months a significant deterioration had occurred, though this deterioration was at a slower rate than occurred before the use of mist tents.

The use of ultrasonic nebulizers for prophylactic therapy is being studied by the Cleveland group, in the hope that if efficient mist therapy can be instituted before pulmonary disease has developed and can be continued throughout life, then the patient might remain free of pulmonary involvement.

In appraising the impressive results of the Cleveland workers it must be remembered that their programme of management involves much more than sleeping in mist tents at night. Clinical assessment is made at 4–6 weekly intervals; attention is paid to the bacteriology of the respiratory tract, antibiotics are prescribed on the results of sensitivity tests, in high dosage both prophylactically and therapeutically, and the importance of regular physiotherapy two or three times daily at home is emphasized.

Phelan *et al.* (1969) in Melbourne treated a group of infants with CF with systemic antibiotics and intermittent aerosol inhalation (by face mask) containing bronchodilators and antibiotics. Pulmonary function tests showed that before treatment there was an increased thoracic gas volume and reduced conductance, which returned to normal after treatment. They suggested that reversal to normal pulmonary function could be achieved without the use of mist tents, and that intermittent aerosol might be a satisfactory alternative to mist tents.

There has only been one study in this country using mist tents, which was briefly reported by Norman at the 5th International CF Conference, Cambridge (1969). He had run a controlled trial with 20 families divided into two groups. All the patients had some established lung damage. Over a period of 2 years he was unable to show any difference between the two groups. He was not prepared to dismiss the value of mist therapy but did consider it a difficult form of treatment for parent, child, and doctor.

Therefore when considering mist tent therapy in CF we have to divide the patients into those with significant pulmonary involvement and those without. In those already with pulmonary involvement, mist tent therapy may slow the progression of pulmonary change, but this can also be achieved without mist tents, as was reported from the late Dr. Winifred Young's clinic in London (Young and Jackson, 1966). It must therefore be decided whether there is in the mist therapy group an improvement in health or a significant increase in survival time to make all the additional disturbance of a mist tent worth while to the patients and to the child. At the Cambridge Conference it emerged in discussion that many paediatricians were having second thoughts about mist therapy, as they had found that about half of adolescent CF patients brought up on nocturnal mist tent therapy abandoned all treatment as soon as they were old enough to look after themselves.

The group of patients without pulmonary involvement poses a different problem. This includes cases diagnosed early in infancy, because of meconium ileus, or because an elder sib is a known case of CF. These patients can be symptom free, and no abnormality need be detected on clinical or radiological examination for years, but specialized pulmonary function tests may detect changes in RV or TLC. In this group Matthews has found a return towards normal of these values after introduction of mist tents, and this therapy may prevent pulmonary changes. Matthews (1969) considers that only 10% of this group show evidence of progressive lung disease over a follow-up period, the average duration of which was 7 years (Matthews, 1969). It is therefore in this group that mist tent therapy may have most to offer.

In a chronic and incurable disease parents and physicians will clutch at any straw. The medical profession has a moral duty not to withhold treatment if it is of proved benefit, but should ask what

is expected from the use of mist tents. Before instituting this regimen the physician should have a clear idea of what he is asking of his patient, of the family, and of himself. In the United Kingdom the financial burden will not fall directly on the family, but mist tents are initially expensive, and if they are not serviced and maintained in working order the initial outlay is wasted and effective treatment is not given. It is only too well known in hospitals that any apparatus involving high humidity is easily contaminated by bacteria, especially pseudomonas. This organism in any case easily invades the lungs of patients with CF, and with the tent and nebulizer this risk may be increased—is this also going to increase the complications with pseudomonas?

Before all patients with CF are provided with mist tents, it seems that paediatricians should decide what they consider to be adequate treatment at the present time and assess the results to date. A well-controlled trial would need to be organized, realizing that in a disease whose natural course is so variable there is going to be no quick answer. In the early treated group the only abnormality which may be present may be a change in lung volumes, which are difficult to measure without expensive apparatus, especially in patients under 5. Such facts will make the results of a trial difficult to assess without a very long follow-up.

Sitting on the fence is rarely a commendable or comfortable posture, and it is one adopted only with reluctant necessity by the present writer after appraisal of the available facts about mist therapy in CF.

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